

Group I: claims 1-11 and 28, drawn to nucleic acids encoding APRIL ligand, vectors, host cells thereof and the expression of recombinant protein.

Group II: claims 12-17, drawn to APRIL polypeptides and pharmaceutical compositions thereof.

Group III: claims 19-21, drawn to antibodies that bind to APRIL ligand polypeptides.

Group IV: claims 22-25, drawn to methods for preventing or reducing the severity of an autoimmune disease, and methods for preventing or reducing the severity of an immune response to a tissue graft, comprising the administration of APRIL ligand polypeptides.

Group V: claims 26 and 41-42 in part, drawn to methods for treating cancer and a method for suppressing the growth of a tumor cell comprising the administration of APRIL ligand polypeptides. The Examiner indicates that claims 41 and 42 will be examined with this group to the extent that they read on the administration of APRIL ligand polypeptide.

Group VI: claim 27, drawn to a method of identifying a receptor for APRIL comprising detecting the binding of a labeled APRIL or a labeled APRIL fragment with a receptor.

Group VII: claims 29-31, drawn to methods for treating a disorder related to APRIL in a mammal comprising introducing a vector comprising APRIL and expressing APRIL in the mammalian cell.

Group VIII: claims 32-35, drawn to methods for inducing cell death and methods of treating, supressing, activating or altering an immune response comprising the administration of an agent capable of interfering with the binding of APRIL to a receptor.

Group IX: claims 36-40 and 41 and 42 in part, drawn to methods of treating, suppressing or altering the

progression of cancer and methods for suppressing the growth of a tumor comprising administering a blocking agent between APRIL ligand and its receptor capable of interfering with the association. The Examiner has indicated that claims 41 and 42 will be examined with this group to the extent that they read on the administration of antibodies.

In response to this requirement, Applicant elects the subject matter of Group IX, claims 36-42, with traverse, for further prosecution in this application. Applicant makes this election of the claims of Group IX expressly without waiver of his right to file for and obtain claims directed to the non-elected subject matter in divisional or continuing applications claiming priority and benefit herefrom, or from a related application, under 35 U.S.C. § 120. Consistent with this election, applicant has canceled without prejudice claims 1-35 and amended claims 42 and 43. These amendments do not add any new subject matter.

The Examiner alleges that the methods of Groups IV-IX differ in the method objectives, method steps and parameters, and in the reagents used. Applicant traverses.

The Manual of Patent Examining Procedure (MPEP) states that there are two criteria for a proper requirement of restriction between patentably distinct inventions. The first is that the inventions must be independent or distinct as claimed. The second is that there must be a serious burden on the Examiner if restriction is not required. The MPEP further states that "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to distinct or independent inventions." MPEP § 803.

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Groups IV-IX comprise claims that recite methods for utilizing the biological properties of the interaction

between APRIL and its receptor. Further, Groups IV, V, VIII and IX all comprise claims that recite methods of administering APRIL ligand, or an antagonist, to a patient for the purpose of treating a disorder chosen from a group of disorders supported by the specification (see, e.g., p. 8, 15). The disorders recited in the claims of groups IV, V, VIII and IX include autoimmune diseases, such as tissue graft rejections and other inappropriate immunological activities, as well as cancer and tumor cell growth. Applicants note that the Examiner herself identified Groups IV, V, VIII and IX as all members of class 530; searching these groups together would not be a serious burden.

Applicant further notes that the claims of Groups V and IX are both directed to methods for treating cancer and suppressing tumor cell growth. The only difference is that whereas the claims of Group V recite APRIL ligand polypeptides, the claims of group Group IX recite a blocking agent. Furthermore, both groups may include claims 41 and 42 as filed. Therefore, the point of contention is whether the subject matter of claims 26 and 36-40 may be examined in the same application without seriously burdening the Examiner. Applicant submits that they can.

Claim 26 of Group V is directed to a method for treating cancer comprising administering a pharmaceutical composition comprising APRIL ligand polypeptides. Claims 36-40 of the elected Group IX are directed to methods for treating, suppressing or altering the progression of cancer comprising administering a blocking agent capable of interfering with the association between APRIL and its receptor. Said blocking agents include both modified APRIL ligand polypeptides and anti-APRIL antibodies.

The specification describes blocking agents as comprising:

"soluble APRIL, anti-APRIL antibodies, and anti-APRIL receptor antibodies, or biologically active fragments thereof." See, p. 28.

Furthermore, the specification supports using APRIL ligand polypeptides, inter alia, as blocking agents:\*

"The invention also provides for reduction of the protein binding domains of the claimed polypeptides or their receptors, to generate mimetics, e.g. peptide or non-peptide agents. The peptide mimetics are able to disrupt binding of APRIL with its respective receptor." Emphasis added. See, p. 26.

Thus, soluble APRIL ligand polypeptides, anti-APRIL antibodies, and anti-APRIL receptor antibodies are all blocking agents. Therefore, because searching groups V and IX together would not be a serious burden on the examiner, applicant believes that Groups V and IX should be examined together.

Applicant further notes that the claims of Groups VIII and IX are both directed to methods for the administration of an agent capable of interfering with, or blocking, the interaction between the APRIL ligand polypeptide and the APRIL receptor polypeptide. Claims 32-35 recite using this method for inducing cell death and treating, suppressing, activating, or altering an immune response. Claims 36-42 recite using this method for treating, suppressing, or altering the progression of cancer and tumor growth. Furthermore, the Examiner has indicated that the subject matter of Groups VIII and IX both fall within class 530, subclass 387.1. Therefore, because searching groups VIII and IX together would not be a serious burden on the examiner, applicant believes that Groups VIII and IX should be examined together.

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\* APRIL ligand polypeptides may also be used to stimulate normal APRIL mediated pharmacological events. See pp. 8, 26.

For at least the reasons stated above, Applicant disagrees with the Examiner that the claims of Groups V, VIII and IX should be examined separately. Their simultaneous examination would not impose a serious burden on the examiner. Applicant requests that these groups be examined together. If the Examiner does not agree, Applicant requests that the Examiner examine Groups V and IX together. In the alternative, Applicant requests that the Examiner examine Groups VIII and IX together.

#### IV. CONCLUSION

Based on the foregoing remarks, Applicant requests that the Examiner enter the above amendments and examine the pending claims in the present application and allow the claims to pass to issue.

Respectfully submitted,

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## APPENDIX OF AMENDED CLAIMS

The following amendments are being submitted in response to the March 13, 2001 restriction requirement in Application No. 09/520,489:

41. (Amended) A method of suppressing growth of a tumor cell that expresses an APRIL ligand polypeptide, comprising the step of contacting said cell with an effective amount of [an APRIL ligand polypeptide of claims 12-15 or an antibody of claims 19-21] an agent chosen from the list consisting of:

- a. an antibody that binds specifically to said APRIL ligand polypeptide comprising at least about 102 amino acids or a soluble ligand polypeptide thereof;
- b. an antibody that binds specifically to said APRIL ligand polypeptide comprising an amino acid sequence found in amino acids 1-55 of SEQ ID NO:2, a fragment thereof, or a soluble ligand polypeptide thereof;
- c. an antibody that binds specifically to said APRIL ligand polypeptide comprising an amino acid sequence found in amino acids 157-250 of SEQ ID NO:2, a fragment thereof, or a soluble ligand polypeptide thereof;
- d. an antibody that binds specifically to SEQ ID NO:2 or a soluble ligand polypeptide thereof;
- e. an antibody that binds specifically to an amino acid substitution analog of SEQ ID NO:2 or a soluble ligand polypeptide thereof;
- f. an antibody that blocks binding of said APRIL ligand polypeptide to an APRIL receptor polypeptide; and

g. an antibody that binds specifically to said APRIL ligand polypeptide and blocks binding of said APRIL ligand polypeptide to an APRIL receptor polypeptide.

42. A method of suppressing growth of a tumor cell that expresses an APRIL receptor polypeptide, comprising the step of contacting said cell with an effective amount of [a soluble APRIL ligand polypeptide of claims 12-15 or an antibody of claims 19-21 to said subject] an agent chosen from the list consisting of:

- a. an antibody that binds specifically to an APRIL ligand polypeptide comprising at least about 102 amino acids or a soluble ligand polypeptide thereof;
- b. an antibody that binds specifically to an APRIL ligand polypeptide comprising an amino acid sequence found in amino acids 1-55 of SEQ ID NO:2, a fragment thereof, or a soluble ligand polypeptide thereof;
- c. an antibody that binds specifically to an APRIL ligand polypeptide comprising an amino acid sequence found in amino acids 157-250 of SEQ ID NO:2, a fragment thereof, or a soluble ligand polypeptide thereof;
- d. an antibody that binds specifically to SEQ ID NO:2 or a soluble ligand polypeptide thereof;
- e. an antibody that binds specifically to an amino acid substitution analog of SEQ ID NO:2 or a soluble ligand polypeptide thereof;
- f. an antibody that blocks binding of an APRIL ligand polypeptide to said APRIL receptor polypeptide; and

g. an antibody that binds specifically to an APRIL ligand polypeptide and blocks binding of said APRIL ligand polypeptide to said APRIL receptor polypeptide.